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Serotonin syndrome with fluoxetine plus tramadol

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The serotonin syndrome is a rare but potentially fatal reaction to the combination of a serotonergic agent and a selective serotonin reuptake inhibitor (SSRI) antidepressant[1]. It arises most often when a monoamine oxidase inhibitor is given with an SSRI[2]. Tramadol is an analgesic commonly used in patients with chronic pain, who are often receiving an SSRI as well. Tramadol inhibits the reuptake of serotonin and the serotonin syndrome has been reported when it was given with the SSRIs paroxetine and sertraline[3,4]. We report a case with fluoxetine.

CASE HISTORY

A woman aged 31 attended casualty with a ten-day history of involuntary tremor of her right hand which had progressively deteriorated and spread to her face. She had a right-sided headache. Her medical history included fibromyalgia, for which she had taken fluoxetine 20 mg daily for three years, and endometriosis. Four weeks earlier she had started taking tramadol 50 mg four times a day for abdominal pains related to endometriosis, and after two weeks her general practitioner had increased the dose to 100 mg four times daily. There was no family history of note.

On examination she was conscious and oriented but greatly agitated and distressed. There was marked twitching of her face with blepharospasm, and she had a slow 2 Hz tremor of her right arm. She was pyrexial (37.9 °C) and sweating. Her cranial nerves were normal and no cerebellar or long tract signs were present. There was some difficulty in articulation, with stuttering speech due to facial twitching.

The symptoms fluctuated, and exacerbations were marked by great anxiety and vigorous almost hysterical movements. On admission, contrast computed tomography of the head and cerebrospinal fluid examination were normal, as were the results of routine haematological and biochemical tests. Serum prolactin was greatly raised (>4500 mU/L). She was given procyclidine, clonazepam and diazepam but these had little effect. On the supposition that the movement disorder was drug-induced, the fluoxetine and tramadol were discontinued. The twitching persisted but began to lessen seven days after admission. She was subsequently discharged home. At no stage during her illness was a neuroleptic given. In the outpatient clinic three weeks later she reported occasional stutters and tremors but was much better; serum prolactin was within the normal range (228 mU/L). Two months later she had fully recovered.

COMMENT

The serotonin syndrome can be difficult to diagnose since the features are non-specific and can be mimicked by various neurological, metabolic and toxicological states. In our patient even a hysterical reaction was considered. Suggested diagnostic criteria include the presence of at least three of the following features: agitation, tremor, mental state changes (e.g. confusion, hypomania), myoclonus, hyperreflexia, fever, shivering, diarrhoea, diaphoresis, and incoordination.[1] Our patient exhibited agitation, tremor, fever and shivering. Infections, metabolic causes, and substance abuse or withdrawal should be excluded and the criteria specify that a neuroleptic should not have been started or increased in dosage before the onset of symptoms.

Patients usually respond fully to discontinuation of the implicated drugs. In our case the long washout period of fluoxetine resulted in a protracted course despite

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discontinuation of the tramadol. Specific antiserotonergic drugs such as cyproheptadine have been suggested as useful treatments in severe cases but clinical experience is limited[5].

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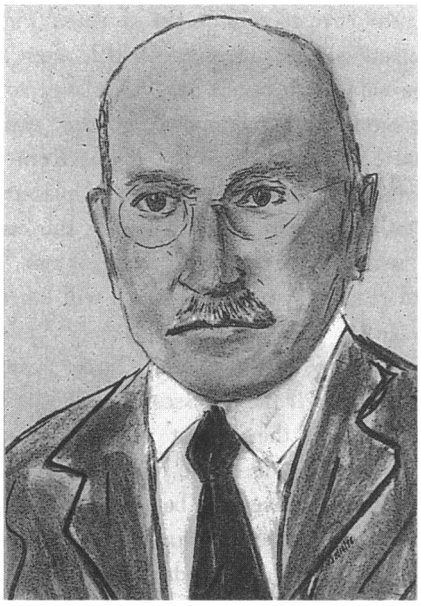

Carl Koller

This month in history

While the mystical and pleasurable properties of the 'Divine plant of the Incas' were known for centuries in South America, it was a 27-year-old ophthalmologist, Carl Koller (1857–1944), who rocked the world by bringing cocaine into clinical practice as a local anaesthetic. Koller's friend and contemporary Sigmund Freud drew to his attention 'the ability of cocaine to render mucus membranes insensitive'. Koller immediately realized that this might be the answer to his quest for a drug which could produce local anaesthesia when instilled into the conjunctival sac. Koller began experimenting and discovered that adding a few drops of cocaine to an animal's eye rendered it insensitive to chemical, mechanical, thermal and electrical stimuli. He tested it on animals and on himself. While he himself was not in attendance, Koller's work was presented by his friend Josef Brettauer on 15 September 1884 at a meeting of the German Ophthalmological Society in Heidelberg. Brettauer instilled a few drops of Koller's solution into a patient's eye. The patient's declaration that he felt nothing marked the end of the era of operating on the eyes of writhing and screaming patients and ushered in the dawn of a new era in anaesthesia.

Venita Jay